Comment on the Reproductive Toxicity of Cannabis and Cannabis-Related Chemicals

Prepared by Suzaynn F. Schick, PhD, Associate Professor of Medicine, University of California, San Francisco

The California Environmental Protection Agency should add cannabis and cannabis-related chemicals to the list of chemicals known to cause reproductive toxicity, as mandated by proposition 65. While there are relatively few high quality studies of the reproductive health effects of cannabis use, it is commonly smoked and smoke is a well-known reproductive toxicant.

Cannabis is typically smoked differently than tobacco, with users less likely to use it daily (1) and often taking fewer puffs and holding each puff in the lungs for longer than cigarette smokers. However, cannabis smoke and tobacco smoke are chemically similar(2) and it is very likely that the health effects that are both A) attributable to both active and passive exposure to tobacco smoke and B) not clearly attributable strictly to the biological effects of nicotine are possibly also caused by exposure to cannabis smoke.

Smoking cigarettes during pregnancy causes fetal growth restriction, resulting in lower birth weight and an array of associated health problems that extend throughout life. Kharrazi et al. showed that active cigarette smoking during pregnancy causes a mean overall decrease in birth weight of 327 g compared to nonsmokers(3). The same study showed that light smoking and exposure to secondhand cigarette smoke cause a mean overall decrease in birth weight of 109 g, after adjustment for gestational age and a number of other variables. The use of smokeless tobacco causes only modest effects on birth weight (4-7). Thus, the toxic combustion products that are present in both tobacco smoke and cannabis smoke, such as carbon monoxide and polycyclic aromatic hydrocarbons, are thought to cause the damage (8).

Sudden infant death syndrome (SIDS) has also been shown to be caused by both active smoking and exposure of the infant to secondhand smoke (SHS) (9-11). It is very important to note that even at the lower levels of exposure that are typical of secondhand exposure, exposure to SHS almost doubles the risk of SIDS (10). Active smoking by mothers, prior to delivery, is believed to cause 20-30% of all SIDS deaths (8).

Cannabis is used in a number of ways that do not result in outright combustion, that also create aerosols that may contain toxic chemicals. Cannabis flowers can be ground and heat-aerosolized in a process often referred to as “vaporizing”. To date, studies of vaporized cannabis flowers have focused primarily on delta-9 tetrahydrocannabinol (THC) delivery and bioavailability. There are no publications in the open scientific literature of the chemical makeup of vaporized cannabis flower aerosol. However, Pomahacova et al. compared the percentage of non-cannabinoid chemicals in vaporizer aerosol and smoke from combustion of a cannabis cigarette (12). Their findings show that chemical content of the vaporized aerosol is temperature-dependent, with higher masses of both cannabinoids and non-cannabinoid chemicals with increasing temperature. At 230° C there were ~20 mgs of non-cannabinoid chemicals in the aerosol for each gram of cannabis vaporized. This compared to ~60 mgs of non-cannabinoid chemicals per gram of cannabis smoked.

Pomahacova et al. also found that temperatures below 230° C were significantly less effective at decarboxylating the dominant cannabinoid in the flowers, tetrahydrocannabinolic acid (THCA), to yield

the psychoactive cannabinoid, THC. Relatively few cannabis vaporizers on the market today have accurate temperature indicators and may exceed this minimum temperature. Typical combustion temperatures in a tobacco cigarette range from 900° C, in the center of the coal, during a puff, to approximately 600° C during the smoldering phase (13). The chemical reactions that create new, potentially harmful chemicals do not cease when the temperature drops below that required for the exothermic reactions that characterize combustion.

Cannabis concentrates can also be consumed by heating to temperatures below combustion. Dabbing is the practice of placing small quantities of cannabis concentrates on a heated surface and inhaling the aerosols. Concentrates can also be consumed using a vape pen or electronic cigarette. However, because most concentrates are very viscous or semi-solid at room temperature, they are typically diluted with more fluid materials so they will wick in a vape pen. Preliminary chemical analyses of dabbing concentrates show that it is an efficient method for decarboxylating THCA and delivering THC for pulmonary administration but did not analyze the chemical makeup of the aerosol (14). Chemical analysis of the aerosol formed by dabbing terpenes, a family of chemicals present in concentrates, shows that dabbing can form methacrolein, benzene and 1,3-butadiene, which are also present in combustion aerosols (15).

In summary, there is significant evidence suggesting that cannabis smoke is a reproductive toxicant. It is chemically similar to cigarette smoke, which is known to cause fetal growth retardation and SIDS. Lower temperature aerosolization methods of use can also create toxic chemicals. Because cannabis has scientifically validated medical uses, many members of the public think that it is harmless. Identifying cannabis smoke as a reproductive toxicant will advance the public health by offering an honest caution about the overall health effects of using cannabis.

1. Compton WM, Han B, Jones CM, Blanco C, Hughes A. Marijuana use and use disorders in adults in the USA, 2002-14: analysis of annual cross-sectional surveys. Lancet Psychiatry. 2016;3(10):954-64.
2. Moir D, Rickert WS, Levasseur G, Larose Y, Maertens R, White P, et al. A comparison of mainstream and sidestream marijuana and tobacco cigarette smoke produced under two machine smoking conditions. Chem Res Toxicol. 2008;21(2):494-502.
3. Kharrazi M, DeLorenze GN, Kaufman FL, Eskenazi B, Bernert JT, Jr., Graham S, et al. Environmental tobacco smoke and pregnancy outcome. Epidemiology. 2004;15(6):660-70.
4. England LJ, Levine RJ, Mills JL, Klebanoff MA, Yu KF, Cnattingius S. Adverse pregnancy outcomes in snuff users. American journal of obstetrics and gynecology. 2003;189(4):939-43.
5. England LJ, Kim SY, Shapiro-Mendoza CK, Wilson HG, Kendrick JS, Satten GA, et al. Effects of maternal smokeless tobacco use on selected pregnancy outcomes in Alaska Native women: a case-control study. Acta Obstet Gynecol Scand. 2013;92(6):648-55.
6. Steyn K, de Wet T, Saloojee Y, Nel H, Yach D. The influence of maternal cigarette smoking, snuff use and passive smoking on pregnancy outcomes: the Birth To Ten Study. Paediatric and perinatal epidemiology. 2006;20(2):90-9.
7. Gupta PC, Subramoney S. Smokeless tobacco use and risk of stillbirth: a cohort study in Mumbai, India. Epidemiology. 2006;17(1):47-51.
8. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.

The health consequences of smoking - 50 years of progress: a report of the Surgeon General. Atlanta, GA; 2014.
9. Anderson HR, Cook DG. Passive smoking and sudden infant death syndrome: review of the epidemiological evidence. Thorax. 1997;52(11):1003-9.
10. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, Coordinating Center for Health Promotion, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health. The health consequences of involuntary exposure to tobacco smoke: a report of the Surgeon General. Atlanta, GA; 2006.
11. American Academy of Pediatrics Task Force on Sudden Infant Death Syndrome. SIDS and other sleep-related infant deaths: expansion of recommendations for a safe infant sleeping environment. Pediatrics. 2011;128(5):1030-9.
12. Pomahacova B, Van der Kooy F, Verpoorte R. Cannabis smoke condensate III: the cannabinoid content of vaporised Cannabis sativa. Inhal Toxicol. 2009;21(13):1108-12.
13. Jenkins RA, Guerin MR, Tomkins BA. Chemistry of environmental tobacco smoke: composition and measurement. 2nd ed. Center for Indoor Air Research, Eisenberg M, editors. Boca Raton, FL: CRC Press; 2000. 467 p.
14. Hadener M, Vieten S, Weinmann W, Mahler H. A preliminary investigation of lung availability of cannabinoids by smoking marijuana or dabbing BHO and decarboxylation rate of THC- and CBD-acids. Forensic Sci Int. 2019;295:207-12.
15. Meehan-Atrash J, Luo W, Strongin RM. Toxicant Formation in Dabbing: The Terpene Story. ACS Omega. 2017;2(9):6112-7.